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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/066,496	01/31/2002	Eldon Emberly	15157	5187

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EXAMINER	
MORAN, MARJORIE A	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 11/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/066,496	EMBERLY ET AL.	
	Examiner	Art Unit	
	Marjorie A. Moran	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25 and 28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. All rejections and objections not reiterated below are hereby withdrawn. Claims 1-25 and 28 are pending.

Claim Rejections - 35 USC § 112

Claims 1-25 and 28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

Steps of identifying sets of stacks that have no known counterpart, and of "representing" backbone configurations which have been thus identified, as recited in amended claim 1, are new matter, as previously set forth.

Applicant's arguments filed 8/28/06 have been fully considered but they are not persuasive. In response to the argument that the specification discloses identifying stacks with no "natural" counterpoint, and that "natural" is the same as "known," it is noted that "natural" and "known" are NOT viewed by those skilled in the art of protein chemistry, computer modeling and/or crystallization as being the same in meaning or scope. In general, "natural" is interpreted to mean "naturally occurring" or "as found in nature" or "wild type." Proteins which are not usually considered to be "natural" by those skilled in the art are those proteins/sequences/ structures which have not been subjected to mutation, crystallization, or combination (e.g. in a fusion protein), nor do

those skilled in the art generally refer to proteins which are synthesized by machine or expressed from a cell system as "natural", even where the proteins still comprise the original or "natural" sequence. By contrast a "known" protein, sequence, or structure is ANY which is known, whether "natural" or not. For example, a fusion protein with a published sequence is certainly KNOWN, but would not be considered by those skilled in the art to be "natural." While applicant may be his own lexicographer, the definition of terms with a meaning different from that known in the prior art must be clearly set forth. No such definition has been found in the originally filed specification and applicant does not point to one. Further, not all "natural" sequences are known, while the list of "known" proteins certainly includes those which are "natural" and those which are NOT "natural," as evidence by the inclusion of combinatorially produced proteins in the NCBI database. Thus, "known" and "natural" are not considered by those skilled in the art to have the same meaning, and are different in scope. The originally filed specification discloses only comparison to "natural" counterparts, but dos NOT discloses comparison to "known" counterparts. Applicant does not, in fact, point to support for either his definition of "natural" (i.e. as being the same as "known" nor to support for comparison to "known" counterparts, therefore the examiner maintains that this step is new matter.

In response to the argument that "means" for comparing and identifying were available to one skilled in the art, based on the knowledge of the prior art, are not germane to a lack of written description rejection. Applicant is reminded that the rejection is not one of enablement, but is one of lack of written description. A full and complete written description of the CLAIMED invention must be supplied by the

originally filed disclosure; while knowledge of the prior art may relied upon for enablement, the same is not the case for written description.

With regard to an "identification" step, applicant points to support for a step of comparing stacks to natural structures. Nowhere does Figure 3 or page 23 provide support for identifying those structures which have no "natural" counterparts, nor specifically, for those with no "known" counterparts. In fact, as all structures in Figure 3 fall into a KNOWN class of structures, it appears that ALL of the stacks of Figure 3 are those which HAVE "known" counterparts. Thus even if the comparison shown in Figure 3 were interpreted to be an "identification" (which it is not), the Figure certainly does not provide support for "identifying" stacks "that have no known counterpart."

In response to the argument that the instant specification does not teach "the opposite" of the claimed invention because the claimed method has relevance and utility in the "real world,", applicant is reminded that the rejection is not one of lack of utility under 35 USC 101, but is one of lack of written description under 35 USC 112. The argument that if one can identify stacks having known counterparts, then one can identify those without known counterparts is again directed to enablement. Applicant is again reminded that the rejection is made over a lack of written description. Just because one CAN do something does not mean that one skilled in the art, based on the disclosure of the originally filed specification indicated, would have recognized this as an embodiment include in applicant's disclosed invention. In fact, the overall disclosure of the instant specification is directed to finding those stacks which MATCH a natural structure (or "counterpart"), as previously set forth. Applicant does not point to support

anywhere for a disclosure of identifying a set of stacks that have "no known counterpart," but only argues that as the comparison to "natural" counterparts IS taught, the obverse was also taught. This is not the case. In a method of finding those stacks with natural counterparts, one may stop when a "match" to a natural structure is found; one need not perform a comparison with ALL natural structures/configurations. However, in order to identify stacks WITHOUT a natural counterpart, the stacks MUST be compared to ALL naturally occurring structure/configurations before one can make a determination that the stacks do not have a natural counterpart. To identify stacks with no known counterpart requires yet more comparison; i.e. to all KNOWN structures, whether natural or not. Thus, the examiner does not agree that a disclosure of steps for performing a comparison to natural structures is necessarily also a disclosure for identification of structures with no known counterparts.

In response to the argument that step (e) of representing backbone configurations is "an inevitable concluding step," it is noted that a computer program, for example, performs ONLY those steps/commands which have been included in the program. If the program does not comprise a command to "display" or "save to a file" than the results will NOT be displayed or saved to a file. While Figure 3 is admitted to be a representation of stacks, it is a representation of at least 4 types of stacks, ALL of which are "identified" as HAVING known counterparts, and thus does not provide support for representing stacks which have been identified as "having no known counterparts" as required by step (d) of claim 1. To further elucidate, while the originally filed disclosure DOES provide support for a step of "representing" stacks, it does NOT

provide support for representing only those stacks identified as "having no known counterparts," as recited in instant claim 1.

For these reasons and those previously set forth, the examiner maintains that support for steps (d) and (e) of pending claim 1 are not supported by the originally filed disclosure and are new matter, and maintains the rejection.

Claim Rejections - 35 USC § 112, 2nd para

Claims 1-25 and 28 are again rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant's arguments filed 8/28/06 have been fully considered but they are not persuasive. The arguments are addressed as they pertain to individual rejections, below.

Claim 1 recites a step of identifying stacks with no "known counterpart". It is unclear what is intended as a "known" counterpart; i.e. structures in "known" proteins; any "known" tertiary configuration of a peptide or isolated domain or subunit of a protein, a specific domain (e.g. a "counterpart" domain only) of a "known" protein, etc. In response to the argument that the meaning of "known" is clear based on page 22 of the specification, it is noted that page 22 does not define, or even disclose, the term "known" anywhere. The specification does not clearly define a "known counterpart" anywhere. With regard to "counterparts," applicant argues that this term refers to "single, known protein domains" or may mean a structure "which has the same fold."

As a "domain" often refers to a site of activity (e.g. a binding site or a site where enzymatic cleavage of polymerization takes place may be referred to as "domains" even where the 3D structure/fold/configuration is unknown) or a particular sequence (e.g. a CCAAT domain, again without any reference to the 3D structure or folds), it is still unclear what applicant intends a "counterpart." As it is still unclear what is intended to be a "known counterpart" to an evaluated stack, claim 1 is indefinite.

Applicant is thanked for clearly setting forth what applicant intends as "representing" on page 16 of the response; i.e. 3D coordinates in a graphical display, in a file, and/or as dihedral angles defining the 3D coordinates. In view of applicant's definition, the rejection with regard to this term is hereby withdrawn.

Amended claim 24 limits claim 1 to one which includes "the reduction" of an amino acid sequence to its "hydrophobicities". It is unclear what is intended by a "reduction" of an amino acid sequence. In response to the argument that the "reduced sequences" are strings of real number connoting relative hydrophobicities or polarities of the amino acid sequences, it is noted that no limitation with regard to "strings of real numbers" is recited in the claims anywhere. In fact, claim 24 explicitly recites that each amino acid **sequence** is reduced to the hydrophobicities of its individual **amino acids**. An amino acid sequence, by definition, is the sequence or ordered "string" of AMINO ACIDS, not numbers. While amino acids are commonly represented by single letters, they are not generally represented as numbers by those skilled in the art. Applicant points to pages 16-17 of the specification for the "concept of reduction". Pages 16-17

disclose that hydrophobic values for amino acids may be calculated and used to determine the energy of a particular stack. While the phrase "reduced to a series of hydrophobicities" is recited on page 16, the specification does not, in fact, define the phrase nor clearly set forth what steps are necessarily included in such a "reduction." If applicant intends that a sequence be "represented" by a "string of real numbers" corresponding to or connoting hydrophobic values calculated for each amino acid in the sequence, then this is not clear from the language of the claim. It is noted that claim 23, from which claim 24 originally depended, recites a step of generating a set of amino acid sequences consisting of hydrophobic and polar amino acids; however, claim 24 no longer depends from claim 23, and claim 23 does not recite that the sequences generated are a "string of real numbers," thus even if claim 24 were to depend from claim 23, the limitation intended for a "reduction" to hydrophobicities recited in claim 24 would still be unclear. As the phrase "reduction to...hydrophobicities" is still unclear, the rejection is maintained.

Claim 28 recites the phrase "with said stack as the lowest energy state", which is nonsensical. A stack may represent the lowest energy state of a particular amino acid sequence, but a stack is not an energy state, per se. It is still unclear what limitation of a stack and/or amino acid sequences is intended. Applicant argues that claim 28 clearly recites that a stack "that accommodates a threshold number of amino acid sequences" in the lowest energy state is considered to be highly designable. In fact, claim 28 does not recite a "threshold number of amino acids," nor does it recite stacks which "accommodate ammoniac ids sequences." What claim 28 actually recites is

amino acids sequences "with" a stack, which does imply some relationship between a stack and amino acid sequences; however, this relationship is not further limited in the claim.

Claim 28 further recites that some limitation "is larger than the average number of sequences per stack" in lines 2-3. It is still unclear **what** is intended to be "larger than the average..." therefore, for this reason and for the reason set forth above, the examiner maintains that claim 28 is indefinite, and the rejection is maintained.

As none of the limitations of claim 28 are clear, claim 28 is indefinite. The limitations of claim 28 are so unclear that the examiner can not make any interpretation of the claim, therefore claim 28 is deemed unsearchable and will not be further examined on its merits with regard to the prior art. Applicant argues that this characterization of the claim was unwarranted and requests that the rejection be withdrawn. While it now appears that the claim is providing some definition of further limitation of what is intended by "highly designable," the limitations intended are still unclear for the reasons set forth above, therefore the rejection is maintained and the claim is still considered unsearchable.

New rejections

Amended claim 1 recites the phrase "high designability" with regard to a set of stacks. The phrase is not defined in claim 1, and the "definition" provided in claim 28 is also unclear for reasons set forth above. The instant specification, on page 9, defines a

"highly designable fold" as one that is the ground state of an "unusually large" number of amino acid sequences. What is intended by "unusually large" with regard to a number of amino acids sequences is not set forth in the specification. As the definition of "highly designability" is based on a relative term which is not itself defined, the "definition" does not clarify what is intended to be a stack of "high designability." As the limitations and meters and bounds intended for a stack of :high designability" are unclear, claim 1 is indefinite. Claims 2-25 depend directly or indirectly from claim 1 and are therefore also indefinite for this reason.

Claim 16 recites the limitation "the starting point" in line 3. There is insufficient antecedent basis for this limitation in the claim, therefore the claim is indefinite. In addition, it is unclear where in the method of claim 1 the "generating" step of claim 16 is intended to occur, therefore claim 16 is further indefinite.

Claim 22 recites the limitation "said cluster" in line 2. There is insufficient antecedent basis for this limitation in the claim, therefore the claim is indefinite. Claim 21 recites clustered stacks, but does not recite any single, particular cluster which would be an antecedent for "said cluster" of claim 22.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (571) 272-0720. The examiner can normally be reached on Monday-Friday; 6 am-2:30 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571)272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Marjorie A. Moran
Primary Examiner
Art Unit 1631

Marjorie A. Moran
11/12/04